

## Amendment and Response

Dkt. 7164.01

I. Rejection of Claims 91 and 92 under 35 U.S.C. § 112, Second Paragraph

Claims 91 and 92 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject which applicant regards as the invention.

Claim 91 was amended to remove the mica limitation and mica was added to the Markush group of claim 92, thereby obviating the basis for this rejection.

Reconsideration and withdrawal of this rejection is respectfully requested.

II. Rejection of Claims 56-63, 65, 67, 68 and 75-78 and 81 under 35 U.S.C. § 102(a)

Claims 56-63, 65, 67, 68 and 75-78, and 81 are rejected under 35 U.S.C. § 102(a) as being anticipated by Dontha et al. J. Pharm. Biomed. Analysis (February 1999) 19:83-91 (hereinafter "Dontha"). Applicants respectfully traverse this rejection.

In order for Dontha to anticipate the claims, each claimed element must be disclosed in the same. The claims to the present invention, however, point out novel features not taught in Dontha. Because each of dependent claims 56-63, 65, 67, 68, 75, 77-78, and 81 each depend directly or indirectly from independent claims 56 and 76, the patentability of the dependent claims depends on the patentability of these independent claims; therefore only independent claims 56 and 76 are discussed below. Each of the below arguments apply *a fortiori* to the dependent claims.

Dontha creates lines by using an HeCd laser at 325 nm to generate an interference pattern. These photopatterned lines created by the laser are domains. It is Applicant's understanding that Dontha is interpreted to show that every attached avidin attached on the line is a domain regardless of the fact that the avidin is *randomly* placed on the biotin surface. Dontha, however, still does not teach, suggest, or make obvious the present invention in view of the arguments presented below.

Claims 56 and 76 are directed to a discrete molecular deposition domain wherein the domain is deposited on the substrate or surface "at a pre-selected location" (emphasis added). Page 24 of the specification, among others, provides support for the "pre-selected" limitation of claims 56 and 76 by stating that because of "the fine control of the deposition device 40 that may be possible with the AFM instrumentation, the exact spot in which the deposition takes place

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may be noted." Furthermore, page 14 of the specification provides support that the domains are discrete by stating that the boundary of the deposition domain is defined by "the material placed thereon." Claiming a molecular array with domains that are attached at a pre-selected location during the deposition process provides clear structural differences over Dontha, which creates domains at any random point on the surface of the substrate and the location of the domain is only known after the deposition has occurred. Furthermore, Applicant has emphasized that the domains on the substrate are physically separate in nature by adding the word "discrete" to the claim.

During the interview of April 11, 2002, Examiner Fredman and Applicant concluded that such language would overcome the concerns surrounding Dontha. Therefore, Applicant has amended claims 56 and 76 in view of those helpful discussions.

Since Dontha does not teach or suggest all the elements of the claimed invention in independent claims 56 or 76, Dontha does not anticipate the present invention.

### III. Rejection of Claims 56-63, 65-85, and 89-90 under 35 U.S.C. § 103(a)

Claims 56-63, 65-85, and 89-90 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Dontha in view of Eggers and further in view of Brenner. Applicants respectfully traverse this rejection. Claims 57-63, 65, 67-75, 77-82, 84-85, and 90 depend directly or indirectly from independent claims 56, 66, 83, and 89. The arguments presented below therefore apply *a fortiori* to the dependent claims.

The arguments presented above with regard to Dontha are reiterated here and are incorporated in their entirety. Dontha does not teach, suggest, or disclose the elements of the claimed invention, alone or in combination with Eggers. Again, the arguments presented below are in view of the helpful discussions held with Examiner Fredman and Applicant on April 11, 2002. The amendments to the claims were a direct result of those discussions in which agreement was reached that such changes would obviate pending concerns.

Eggers discloses "an array 12 of test sites 14" that include "detection circuitry 16 and recognition circuitry 18" Col. 3, lns. 63-63. The test sites further include a well 20 and probes 26 formed within the well 20. See Figures 1-3. More importantly, Eggers utilizes photolithography

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to form wells 20 *in* the substrate 22. See Figures 2-3, 6 and 7. The combination of Dontha and Eggers therefore does not make the claimed invention obvious.

Brenner, a tertiary reference, also fails to remedy the deficiencies of both Dontha and Eggers. Brenner discloses "a method of labeling and sorting molecules, particularly polynucleotides." Col. 6, lns 12-13. Brenner, however, teaches "discrete regions" in which "the regions range in area from several  $\mu\text{m}^2$ , e.g. 3-5, to several hundred  $\mu\text{m}^2$ , e.g. 100-500." Col. 12, lns 51-57. The Examiner relies on Brenner to teach "the placement of alkanethiolates onto solid supports." Office Action, pg. 5.

In stark contrast to the teachings of Dontha, Eggers, and Brenner, the present invention does not require that wells be mechanically ablated *into the substrate* to provide a deposition site. The present claims claim a discrete domain that is "deposited **on** the substrate at a pre-selected location" (claims 56, 83, 89, and 91, emphasis added) and "deposited at a pre-selected location **on the surface**" (claim 76, emphasis added). Therefore, the present invention provides domains on an unablated substrate not having wells (depressions in the substrate), as opposed to Eggers, that are deposited at a pre-selected location, as opposed to Dontha, and which may be used for characterizing molecular interaction events, as opposed to Brenner. Dontha, Eggers, and Brenner, alone or in combination, therefore do not teach, disclose, or suggest the present invention of creating domains on a substrate at pre-selected locations.

In addition, claims 83 and 89 further require "at least two domains containing different biologically or chemically based molecules." Dontha, Eggers, and Brenner, alone or in combination, do not teach the formation of an array that includes domains having two different molecules. In fact, Dontha directly teaches away from the creation of an array with different molecules in different domains because of how the avidin material is deposited **on the surface**. Eggers and Brenner could not be properly combined with Dontha to correct this deficiency in the Dontha reference.

Dontha, Eggers, and Brenner, alone or in combination, fail to teach, disclose, suggest, or provide any motivation such that one skilled in the art would make the claimed invention. Reconsideration and withdrawal of the pending rejection is respectfully requested.

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IV. Rejection of Claims 56-63, 65-85, and 89-92 under 35 U.S.C. § 103(a)

Claims 56-63 and 65-85 and 89-92 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Dontha in view of Eggers and in further in view of Brenner and U.S. Patent 6,255,469 to Seeman. Applicants respectfully traverse this rejection.

The arguments presented above with regard to Dontha, Eggers, and Brenner are reiterated here and are incorporated in their entirety. Seeman fails to remedy the deficiencies of Dontha, Eggers, and Brenner, alone or in combination thereof, to teach or suggest the claimed invention.

Seeman teaches specific polynucleic acid structure that includes helical domains. Seeman further teaches two and three dimensional polynucleic acid nanostructures which are periodic and translationally symmetrical. A crystal lattice DNA structure can be formed using the nanostructures. In one example, imaging is done of the produced materials using an AFM on mica. Seeman, however, does not remedy the deficiencies of Dontha, Eggers, and Brenner, alone or in combination, to teach or suggest an array that includes discrete domains deposited on a surface at pre-selected locations.

Because Seeman, alone or in combination with any of the cited references, fails to provide the teaching or motivation to create the invention claimed in the independent claims. The fact that Seeman teaches the use of mica does not render independent claims 56, 66, 76, 83, or 89 obvious. Claims that depend directly or indirectly from independent claims 56, 66, 76, 83, or 89 are non-obvious.

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**CONCLUSION**

In view of the above amendments and preceding remarks, Applicants respectfully urge that the Examiner's rejections be reconsidered and withdrawn, and that the pending claims be allowed. However, if the Examiner believes that any issues remain unresolved, he is invited to telephone the undersigned to expedite allowance.

Respectfully submitted,

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**MARKED-UP VERSION SHOWING CHANGES****IN THE CLAIMS**

56. (Thrice Amended) A molecular array for characterizing molecular interaction events, comprising:

- (a) a substrate; and
- (b) at least one discrete molecular deposition domain on said substrate wherein the spatial address of the domain is less than one micron in area and each domain includes a biologically or chemically based molecule [directly] deposited on the substrate at a pre-selected location.

66. (Amended) A method for the processing of an array comprising:

- (a) forming an array on a substrate, the array comprising a plurality of deposition domains formed of a deposition material at a pre-selected location;
- (b) exposing the array to one or more materials which contain an at least one target sample that causes a molecular interaction event with one or more of the deposition samples; and
- (c) scanning the array utilizing a scanning probe microscope to characterize the molecular interaction events that have occurred between the target samples and the deposition material.

76. (Amended) An array for the identification of a target material comprising:

- a [silicon] substrate including a substantially flat surface; and
- an at least one discrete deposition domain deposited on said surface, said deposition domain being smaller than one micron in total area and deposited at a [known] pre-selected location on the surface, the deposition domain including a long chain biomolecular deposition material having the capacity to bind the target material.

83. (Amended) An array of deposition domains for the detection of one or more pre-determined target materials comprising:

- a solid glass substrate including a substantially flat surface; and

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an at least one discrete domain deposited on the surface of the substrate, each domain being deposited at a known location and being smaller than one micron in area, each domain further including at least one type of molecule with a binding affinity for one or more of the target materials, at least two domains containing different biologically or chemically based molecules.

89. (Amended) A molecular array for characterizing molecular interaction events, comprising:

(a) a substrate; and

(b) at least one molecular deposition domain on said substrate wherein the spatial address of the domain is less than one micron in area, each domain includes a biologically or chemically based molecule directly deposited on the substrate at a [known] pre-selected location, [and wherein the molecular deposition domain created by a molecular deposition probe having at least one microsphere attached thereto] at least two domains containing different biologically or chemically based molecules.

91. (Amended) A molecular array for characterizing molecular interaction events, comprising:

(a) a substrate [made of mica]; and

(b) at least one molecular deposition domain on said substrate wherein the spatial address of the domain is less than one micron in area, each domain includes a biologically or chemically based molecule directly deposited on the substrate at a [known] pre-selected location, and wherein the molecular deposition domain interacts with a molecular deposition probe having at least one microsphere attached thereto.

92. (Amended) The array of claim 91 wherein the substrate includes a surface chosen from one or more of the group consisting of mica, glass, silicone, tetrafluoroethylene, polystyrene, polycarbonate, and polypropylene.